Chromatin cruise director

Gene expression programs are directed by patterns of gene activation and silencing and are regulated at several levels, including chromatin structural states. The self-renewing skin epithelium contains discrete multipotent progenitor cell populations, and differentiation of these cells is accompanied by increased expression of keratinocyte differentiation and epidermal barrier formation genes within the epidermal differentiation complex (EDC) locus. Mardaryev and colleagues recently demonstrated that this increased transcriptional activity occurs with significant reorganization of the higher-order chromatin architecture at this EDC locus. In fact, this locus is relocated from the nuclear periphery toward the nuclear interior and is associated with SC35-positive speckles, which mark hotbeds of transcriptional activity. This reorganization is regulated, at least in part, by the lineage-specific p63 transcription factor via its direct target Brg1, the ATP-dependent chromatin remodeling factor. These findings will enable additional studies into the chromatin reorganization process during epidermal differentiation. (*Development* 141:101–11, 2014) *Selected by M. Amagai*

All in the family

Hereditary fibrosing poikiloderma (HFP) is a rare autosomal-dominant disease characterized by poikiloderma, tendon contractures, and progressive pulmonary fibrosis described previously in a South African family. This condition differs from other known types of hereditary poikilodermas (Rothmund–Thomson syndrome, Werner syndrome, and Kindler syndrome). Mercier and colleagues identified four additional cases of HFP from French, Algerian, Italian, and Moroccan origins. Whole-exome sequencing analyses revealed three rare heterozygous mutations in the *FAM111B* gene in the affected members of five unrelated families. A *de novo* occurrence in two unrelated families supports the notion that mutations of the *FAM111B* gene cause HFP. Although little is known about the predicted protein product, other documented putative loss-of-function mutations in individuals without HFP suggest that the variations identified in this study are likely gain-of-function or dominant-negative variants. Thus, *FAM111B* is prominently involved in the development of fibrosis, a key pathological process in many diseases. (*Am J Hum Genet* 93:1100–7, 2013) *Selected by J. Uitto*

Pigmentation by Notch

Although loss-of-function mutations in the keratin 5 gene (*KRT5*) have been detected in cases of Dowling–Degos disease (DDD), as many as 50% of cases remain unexplained. In some individuals who had been originally diagnosed with the DDD variant Galli–Galli disease, acantholysis was observed in addition to the symptoms of postpubertal reticulate hyperpigmentation and small hyperkeratotic dark-brown papules. Basmanav and colleagues recently described nine different mutations (nonsense, splice site, missense, insertion, and deletion mutations) in *POGLUT1*, the gene that encodes protein *O*-glucosyltransferase 1 of the Notch signaling pathway, in 13 unrelated individuals with DDD, suggesting that these mutations underlie DDD pathogenesis. Comparison of disease presentation of DDD patients with *KRT5* mutations and those with *POGLUT1* mutations highlights a possible relationship between the mutated gene and the phenotype. The predicted deleterious effects of these identified mutations on *O*-glucosyltransferase 1 protein function emphasize the importance of the Notch signaling pathway in pigmentation and differentiation of the epidermis. (*Am J Hum Genet* 94:135–43, 2014) *Selected by J. Uitto*

Snail invasion

The transcriptional repressor Snail is thought to be a master regulator of the epithelial-to-mesenchymal transition (EMT), which is important in tumor cell dedifferentiation and thus in tumor progression. Evidence abounds regarding the role of Snail in signaling cascades *in vitro*; however, less is known about its role in carcinogenesis and metastasis *in vivo*, especially with regard to skin cancer. Recently, De Craene and colleagues reported that skin-specific Snail transgenic mice develop spontaneous tumors, some of which are characterized by hyperproliferation of sebaceous glands via repression of Blimp-1. Snail expression in keratinocytes promotes cell survival and resistance to genotoxic agents, and Snail synergizes with p53 loss to initiate tumor development, perhaps as a result of persistent damaged DNA. Together, these studies indicate not only that Snail regulates the EMT but also that epidermal Snail expression promotes skin cancer and progression via enhanced cell protection, increased epidermal progenitor cell proliferation, and greater metastatic potential. (*Cell Death Differ* 21:310–20, 2014) *Selected by M. Leverkus*

Onward and upward

Hair follicles (HFs) are tubelike structures that are continuous with the epidermis and contain the hair shaft. Lumen formation, which occurs in many other organs via infolding of a cell sheet, occurs in HFs via a poorly understood mechanism. Veniaminova and colleagues examined the infundibulum, which includes the mouth of the HF, and found that generation of the HF lumen proceeds by early outward movement of keratinocytes from the core of the developing hair buds in the embryo. These cells express keratin 79 (K79) and line the multilayered HF infundibulum. Migration of these cells from the nascent hair germs prior to lumen formation provides a novel mechanism for hair canal morphogenesis. Interestingly, upward movement of stem cells sustains the infundibulum, and disruption of the infundibulum in the case of human acne resulted in loss of expression of K79 from comedones. These studies offer insight into generation of the hollow core of the HF during development. (*Development* 140:4870–80, 2013) *Selected by R. Swerlick*

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